



SUBSTITUTE SEQUENCE LISTING

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TECH CENTER 1330/2900

<110> Anderson, John P.  
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<120> Beta-Secretase Enzyme Compositions and  
Methods

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<150> US 09/501,708

<151> 2000-02-10

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 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
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 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
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Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met
	290					295					300				
Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln
305					310					315					320
Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr
			325					330						335	
Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val
			340					345					350		
Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile
		355					360					365			
Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala
	370					375					380				
Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr
385					390					395					400
Asn	Ile	Pro	Gln	Thr	Asp	Glu									
				405											

<210> 59

<211> 452

<212> PRT

<213> Homo sapiens

<400> 59

Met	Ala	Gln	Ala	Leu	Pro	Trp	Leu	Leu	Leu	Trp	Met	Gly	Ala	Gly	Val
1				5					10					15	
Leu	Pro	Ala	His	Gly	Thr	Gln	His	Gly	Ile	Arg	Leu	Pro	Leu	Arg	Ser
			20					25					30		
Gly	Leu	Gly	Gly	Ala	Pro	Leu	Gly	Leu	Arg	Leu	Pro	Arg	Glu	Thr	Asp
		35					40					45			
Glu	Glu	Pro	Glu	Glu	Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val
	50					55					60				
Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr
65					70					75					80
Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser
				85					90					95	
Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr
			100					105					110		
Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val
		115					120					125			
Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp
	130					135					140				
Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile
145					150					155					160

Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp
				165					170					175	
Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp
			180					185					190		
Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro
		195					200					205			
Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln
	210					215					220				
Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile
225						230				235					240
Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg
				245					250					255	
Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln
			260					265					270		
Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val
		275					280					285			
Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala
	290					295					300				
Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp
305						310				315					320
Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr
				325					330					335	
Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val
			340					345					350		
Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg
		355					360					365			
Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala
	370					375					380				
Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu
385					390					395					400
Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala
				405					410					415	
Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val	Glu
			420					425				430			
Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile	Pro
		435					440					445			
Gln	Thr	Asp	Glu												
			450												

<210> 60

<211> 420

<212> PRT

<213> Homo sapiens

<400> 60

Met	Ala	Gln	Ala	Leu	Pro	Trp	Leu	Leu	Leu	Trp	Met	Gly	Ala	Gly	Val
1				5					10					15	
Leu	Pro	Ala	His	Gly	Thr	Gln	His	Gly	Ile	Arg	Leu	Pro	Leu	Arg	Ser
			20					25					30		
Gly	Leu	Gly	Gly	Ala	Pro	Leu	Gly	Leu	Arg	Leu	Pro	Arg	Glu	Thr	Asp
		35					40					45			
Glu	Glu	Pro	Glu	Glu	Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val
	50					55					60				
Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr
65					70					75					80
Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser
				85					90					95	
Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr
			100					105					110		
Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val
			115				120					125			

Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp
130						135					140				
Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile
145					150					155					160
Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp
				165					170					175	
Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp
			180					185					190		
Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro
		195					200					205			
Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln
	210					215					220				
Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile
225					230					235					240
Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg
				245					250					255	
Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln
			260					265					270		
Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val
	275						280					285			
Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala
	290					295					300				
Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp
305					310					315					320
Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr
				325					330					335	
Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val
			340					345					350		
Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg
		355					360					365			
Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala
	370					375					380				
Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu
385					390					395					400
Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala
				405					410					415	
Val	Ser	Ala	Cys												
			420												

<210> 61

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic peptide inhibitor

<221> MOD\_RES

<222> 4

<223> Xaa = hydroxyethylene

<400> 61

Glu Val Met Xaa Ala Glu Phe

1

5

<210> 62

<211> 26

<212> PRT

<213> Homo sapiens

<400> 62



Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met  
 1 5 10 15  
 Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
 20 25

<210> 63  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> P26-P4'sw peptide substrate

<400> 63  
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
 1 5 10 15  
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu  
 20 25 30  
 Phe

<210> 64  
 <211> 29  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> P26-P1' peptide substrate with CGG linker

<400> 64  
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
 1 5 10 15  
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu  
 20 25

<210> 65  
 <211> 501  
 <212> PRT  
 <213> Mus musculus

<400> 65  
 Met Ala Pro Ala Leu His Trp Leu Leu Leu Trp Val Gly Ser Gly Met  
 1 5 10 15  
 Leu Pro Ala Gln Gly Thr His Leu Gly Ile Arg Leu Pro Leu Arg Ser  
 20 25 30  
 Gly Leu Ala Gly Pro Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160

Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp
				165					170					175	
Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp
			180					185					190		
Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Ile	Pro
		195					200				205				
Asn	Ile	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln
	210					215					220				
Thr	Glu	Ala	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile
225					230					235					240
Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg
				245					250					255	
Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln
			260					265					270		
Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val
		275					280				285				
Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala
	290				295						300				
Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp
305					310					315					320
Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr
			325						330					335	
Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val
			340					345					350		
Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg
	355					360						365			
Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala
	370				375						380				
Val	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu
385					390				395						400
Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala
			405					410						415	
Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val	Glu
			420					425					430		
Gly	Pro	Phe	Val	Thr	Ala	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile	Pro
		435				440						445			
Gln	Thr	Asp	Glu	Ser	Thr	Leu	Met	Thr	Ile	Ala	Tyr	Val	Met	Ala	Ala
	450					455					460				
Ile	Cys	Ala	Leu	Phe	Met	Leu	Pro	Leu	Cys	Leu	Met	Val	Cys	Gln	Trp
465					470				475						480
Arg	Cys	Leu	Arg	Cys	Leu	Arg	His	Gln	His	Asp	Asp	Phe	Gly	Asp	Asp
			485					490						495	
Ile	Ser	Leu	Leu	Lys											
			500												

<210> 66

<211> 480

<212> PRT

<213> Homo sapiens

<400> 66

Thr	Gln	His	Gly	Ile	Arg	Leu	Pro	Leu	Arg	Ser	Gly	Leu	Gly	Gly	Ala
1				5					10					15	
Pro	Leu	Gly	Leu	Arg	Leu	Pro	Arg	Glu	Thr	Asp	Glu	Glu	Pro	Glu	Glu
			20					25					30		
Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly
			35			40						45			
Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro
	50				55						60				
Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val
65					70					75					80





Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln
1				5					10					15	
Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn
			20					25				30			
Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro
		35				40						45			
His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr
	50				55						60				
Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp
65				70					75					80	
Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn
			85					90					95		
Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe
			100				105						110		
Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala
		115				120					125				
Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu
	130				135					140					
Val	Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly
145				150					155					160	
Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly
			165					170						175	
Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu
		180					185						190		
Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val
	195					200					205				
Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr
	210			215						220					
Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu
225				230					235					240	
Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser
			245					250					255		
Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val
		260					265						270		
Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser
	275					280					285				
Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile
	290				295				300						
Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln
305				310					315					320	
Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val
			325					330					335		
Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala
		340					345					350			
Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu
	355					360					365				
Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu
	370				375						380				
Asp	Cys	Gly	Tyr	Asn	Ile	Pro	Gln	Thr	Asp	Glu					
385				390					395						

<210> 69

<211> 439

<212> PRT

<213> Homo sapiens

<400> 69

Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu
1			5					10						15	
Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr
		20					25						30		

Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His
		35					40					45			
Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys
	50					55					60				
Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly
65				70					75						80
Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala
			85					90						95	
Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser
		100						105					110		
Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro
	115					120						125			
Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His
	130				135						140				
Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu
145				150					155						160
Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly
			165					170						175	
Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile
		180					185						190		
Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn
	195					200						205			
Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser
	210				215						220				
Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe
225				230					235						240
Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe
			245					250						255	
Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly
		260				265							270		
Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly
	275					280						285			
Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr
	290			295						300					
Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys
305				310					315						320
Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile
			325					330						335	
Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly
		340				345						350			
Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala
	355					360					365				
Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn
	370			375						380					
Ile	Pro	Gln	Thr	Asp	Glu	Ser	Thr	Leu	Met	Thr	Ile	Ala	Tyr	Val	Met
385				390					395						400
Ala	Ala	Ile	Cys	Ala	Leu	Phe	Met	Leu	Pro	Leu	Cys	Leu	Met	Val	Cys
			405					410						415	
Gln	Trp	Arg	Cys	Leu	Arg	Cys	Leu	Arg	Gln	Gln	His	Asp	Asp	Phe	Ala
		420					425					430			
Asp	Asp	Ile	Ser	Leu	Leu	Lys									
	435														

<210> 70

<211> 390

<212> PRT

<213> Homo sapiens

<400> 70

Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu
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Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu
50						55				60					
His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg
65				70						75					80
Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu
				85					90					95	
Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg
			100					105					110		
Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly
		115					120					125			
Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg
		130				135					140				
Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr
145				150						155					160
His	Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro
				165					170					175	
Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile
			180					185					190		
Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro
		195					200					205			
Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile
	210					215					220				
Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys
225				230						235				240	
Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val
				245					250					255	
Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys
		260						265					270		
Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala
		275					280					285			
Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met
	290				295						300				
Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln
305				310						315				320	
Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr
				325					330					335	
Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val
			340					345				350			
Ile	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile
		355				360						365			
Gly	Phe	Ala	Val	Ser	Ala										
	370														

<210> 72

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> P10-P4'staD-V peptide inhibitor

<221> MOD\_RES

<222> 10

<223> Xaa is statine moiety

<400> 72

Lys	Thr	Glu	Glu	Ile	Ser	Glu	Val	Asn	Xaa	Val	Ala	Glu	Phe
1				5					10				

<210> 73

<211> 9



<212> PRT  
 <213> Artificial Sequence

<220>  
 <223> P4-P4'staD-V peptide inhibitor

<221> MOD\_RES  
 <222> 5  
 <223> Xaa is statine moiety

<400> 73  
 Ser Glu Val Asn Xaa Val Ala Glu Phe  
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<210> 74  
 <211> 431  
 <212> PRT  
 <213> Homo sapiens

<400> 74  
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 1 5 10 15  
 Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu  
 20 25 30  
 Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly  
 35 40 45  
 Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro  
 50 55 60  
 Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val  
 65 70 75 80  
 Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu  
 85 90 95  
 Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr  
 100 105 110  
 Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro  
 115 120 125  
 His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu  
 130 135 140  
 Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly  
 145 150 155 160  
 Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe  
 165 170 175  
 Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu  
 180 185 190  
 Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala  
 195 200 205  
 Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr  
 210 215 220  
 Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu  
 225 230 235 240  
 Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp  
 245 250 255  
 Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr  
 260 265 270  
 Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile  
 275 280 285  
 Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly  
 290 295 300  
 Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe  
 305 310 315 320

Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe
				325					330					335	
Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val
			340					345					350		
Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser
		355					360					365			
Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val
	370				375						380				
Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His
385					390					395				400	
Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr
				405				410						415	
Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile	Pro	Gln	Thr	Asp	Glu	
			420					425					430		

<210> 75  
 <211> 361  
 <212> PRT  
 <213> Homo sapiens

<400> 75

Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu
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Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr
			20					25					30		
Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His
	35						40					45			
Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys
	50					55					60				
Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly
65					70					75				80	
Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala
				85					90					95	
Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser
		100						105					110		
Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro
	115					120						125			
Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His
	130					135					140				
Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu
145				150						155				160	
Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly
			165						170					175	
Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile
	180							185					190		
Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn
	195					200						205			
Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser
	210				215						220				
Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe
225					230					235				240	
Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe
			245						250					255	
Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly
		260					265						270		
Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly
	275					280						285			
Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr
	290					295					300				
Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys
305					310					315				320	

Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
                           325                          330                          335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
                           340                          345                          350  
 Phe Ala Val Ser Ala Cys His Val His  
                           355                          360

<210> 76  
 <211> 63  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(63)  
 <223> n = A,T,C or G

<400> 76  
 garacngayg argarcnga rgarccnggn mgnmgnggnw snttygtnga ratggtngay 60  
 aay 63

<210> 77  
 <211> 21  
 <212> PRT  
 <213> Homo sapiens

<400> 77  
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
   1                          5                          10                          15  
 Glu Met Val Asp Asn  
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<210> 78  
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<220>  
 <223> Peptide inhibitor P3-P4' XD-V  
 <221> MOD\_RES  
 <222> 3  
 <223> Xaa is hydroxyethylene or statine

<400> 78  
 Val Met Xaa Val Ala Glu Phe  
   1                          5

<210> 79  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 79  
 Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
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<210> 80  
 <211> 419  
 <212> DNA  
 <213> Artificial Sequence

<220>  
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<400> 80  
 ctgttgggct cgcggttgag gacaaactct tcgcggtcct tccagtactc ttggatcgga 60  
 aacccgtcgg cctccgaacg gtactccgcc accgaggac ctgagcgagt ccgcatcgac 120  
 cggatcgga aacctctcga ctgttggggg gagtactccc tctcaaaagc gggcatgact 180  
 tctgcgctaa gattgtcagt ttccaaaaac gaggaggatt tgatattcac ctggcccgcg 240  
 gtgatgcctt tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca 300  
 agcttgaggt gtggcaggct tgagatctgg ccatacactt gagtgacaat gacatccact 360  
 ttgcctttct ctccacaggt gtccactccc aggtccaact gcaggtcgac tctagaccc 419

<210> 81  
 <211> 8  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Peptide inhibitor P4-P4' XD-V

<221> MOD\_RES  
 <222> 4  
 <223> Xaa is hydroxyethylene or statine

<400> 81  
 Glu Val Met Xaa Val Ala Glu Phe  
 1 5

<210> 82  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> APP fragment P5-P4' wt

<400> 82  
 Ser Glu Val Lys Met Asp Ala Glu Phe  
 1 5

<210> 83  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> APP fragment P5-P4'wt

<400> 83  
 Ser Glu Val Asn Leu Asp Ala Glu Phe  
 1 5

<210> 84  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> APP fragment

<400> 84  
Ser Glu Val Lys Leu Asp Ala Glu Phe  
1 5

<210> 85  
<211> 9  
<212> PRT  
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<220>  
<223> APP fragment

<400> 85  
Ser Glu Val Lys Phe Asp Ala Glu Phe  
1 5

<210> 86  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 86  
Ser Glu Val Asn Phe Asp Ala Glu Phe  
1 5

<210> 87  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 87  
Ser Glu Val Lys Met Ala Ala Glu Phe  
1 5

<210> 88  
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<212> PRT  
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<220>  
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<400> 88  
Ser Glu Val Asn Leu Ala Ala Glu Phe  
1 5

<210> 89  
<211> 9  
<212> PRT  
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<220>  
<223> APP fragment

<400> 89

Ser Glu Val Lys Leu Ala Ala Glu Phe  
1 5

<210> 90  
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<212> PRT  
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<220>  
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<400> 90  
Ser Glu Val Lys Met Leu Ala Glu Phe  
1 5

<210> 91  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 91  
Ser Glu Val Asn Leu Leu Ala Glu Phe  
1 5

<210> 92  
<211> 9  
<212> PRT  
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<220>  
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<400> 92  
Ser Glu Val Lys Leu Leu Ala Glu Phe  
1 5

<210> 93  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 93  
Ser Glu Val Lys Phe Ala Ala Glu Phe  
1 5

<210> 94  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 94

Ser Glu Val Asn Phe Ala Ala Glu Phe  
1 5

<210> 95  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 95  
Ser Glu Val Lys Phe Leu Ala Glu Phe  
1 5

<210> 96  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP fragment

<400> 96  
Ser Glu Val Asn Phe Leu Ala Glu Phe  
1 5

<210> 97  
<211> 14  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> APP-derived fragment P10-P4' (D-V)

<400> 97  
Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Val Ala Glu Phe  
1 5 10

<210> 98  
<211> 35  
<212> DNA  
<213> Homo sapiens

<400> 98  
cccgaagagc ccggccggag gggcagcttt gtcga

35

<210> 99  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 99  
Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg  
1 5 10

<210> 100  
<211> 10  
<212> PRT  
<213> Artificial Sequence

<220>  
 <223> Recombinant 293T cells  
  
 <400> 100  
 Thr Gln His Gly Ile Arg Leu Pro Leu Arg  
 1 5 10  
  
 <210> 101  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Recombinant 293T cells  
  
 <400> 101  
 Met Val Asp Asn Leu Arg Gly Lys Ser  
 1 5  
  
 <210> 102  
 <211> 10  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Recombinant CosA2 cells  
  
 <400> 102  
 Gly Ser Phe Val Glu Met Val Asp Asn Leu  
 1 5 10  
  
 <210> 103  
 <211> 4  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> APP substrate fragment:WT Sequence  
  
 <400> 103  
 Val Lys Met Asp  
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 <210> 104  
 <211> 4  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> APP substrate fragment:Swedish Sequence  
  
 <400> 104  
 Val Asn Leu Asp  
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